REMARKS/ARGUMENTS

This is in response to the Office Action mailed January 4, 2006.

Claims 8 and 11 have been amended and claims 5, 12, 13 and 15 have been withdrawn as being based on non-elected species. Support for amendments to claims 8 and 11 can be found throughout the originally filed application, e.g., paragraph 26. No new matter has been added.

Independent claim 1 and its dependent claims 2-4, 6, and 8-10, and independent claims 7, 11 and 14 are currently pending and at issue.

Election - 35 U.S.C. §121

The Examiner asserts that claims 3, 5 and 7 are generic to a plurality of disclosed patentably distinct species comprising health problems and that the Applicant is required to elect a single disclosed species. As the Examiner notes, during a December 20, 2005 telephone conversation, Applicants to expedite prosecution of the case, made a provisional election to prosecute the invention of coronary artery disease.

The Applicants affirm the election of the species coronary artery disease. Claims 1-4, 6-11 and 14 are readable on the elected species. Claims 5, 12, 13 and 15 have been withdrawn. Should the examiner find the elected species patentable, it is then respectfully requested that the non-elected species be examined. The Applicants reserve the right to file a divisional application to all subject matter or claims withdrawn, cancelled or restricted out. The Applicants elect these embodiments with traverse.

Claim Rejections - 35 U.S.C. §103

The Examiner has rejected the claims under U.S.C. § 103(a) as being unpatentable over (1) Summerbell (BMJ 317 1998 p. 1478-89) and Metz et al (AJH 1:58-60 1988), in view of knowledge that allegedly can be obtained by routine experimentation or is well known to one of ordinary skill in the art.

In each of the two rejections, the Examiner has not established a *prima facie* case of obviousness as set forth in MPEP §§ 706.02(j) and 2143. Each cited reference does not teach or expressly or impliedly suggest any of the limitations set forth in the present claims. There is no motivation to combine the references with other knowledge. There would not be a reasonable expectation of success. Moreover, it is inappropriate for the Examiner to take official notice that the other elements can be readily obtain by routine experimentation or are generally known to one of ordinary skill in the art, so as to modify the references to reach the claimed invention.

In addition, the Applicants are submitting a variety of evidence showing the present invention's unexpected results, which has led to a significant shift in the scientific community and the food industry, which has supported and endorsed the methods of the present invention leading to significant recognition and commercial success.

The Examiner has rejected claims 1-4, 6-8, 10, 11 and 14 under U.S.C. § 103(a) as being unpatentable over Summerbell (BMJ 317 1998 p. 1478-89). The Examiner asserts that Summerbell allegedly teaches weight loss in obese patients on a diet comprising milk or yogurt and that it would have been obvious to one of ordinary skill in to formulate a high calcium diet for obese patients to achieve the beneficial effect of a reduction in body fat content in view of the Summerbell.

Currently independent claims 1, 7, 11 and 14 are directed to methods for avoiding or

reducing a health problem, e.g., coronary artery disease, in an individual comprising administering dietary calcium or dairy to reduce that problem, e.g., to induce a metabolic change, e.g., to decrease intracellular calcium concentrations in adipocytes, stimulate lipolysis, inhibit lipogenesis, increase expression of white adipose tissue uncoupling protein 2 (UCP2), reduce serum insulin levels, increase thermogenesis, and/or decrease levels of calcitrophic hormones.

Applicants contend that the present invention is distinct from Summberbell, which does not disclose, teach or suggest any of the elements of independent claims 1, 7, 11 or 14.

As set forth in the introduction, Summerbell tests diets with high compliance and hence good for weight loss. The study in Summerbell was designed to test the hypothesis that prescription of a simple and novel diet would result in higher levels of compliance and weight loss. In fact, Summerbell associates higher weight loss for the milk diet groups because each of the milk diets is "simple but much less boring and patients were more likely to comply with it" than with the conventional diet. In deed, Summerbell is "not advocating milk only as a general long term reducing diet for obese outpatients, because in the long term it will cease to be novel and compliance will fall." Summerbell concludes that "[p]robably the best strategy is to rotate diets..." This statement would lead one away from the teaching of the present invention, which involves the use of sufficient amounts of dairy or calcium, with some claims reciting either daily or monthly dosages. The point to extrapolate from Summberbell is that one could use any type of food regimen or diet so long as it is simple and less boring to ensure compliance. To the contrary, the present invention is directed to methods of reducing a health problem such as coronary heart disease by administering dietary calcium or dairy, in sufficient amounts. Nowhere in Summerbell is a method disclosed for avoiding or reducing a health problem, such as coronary artery disease comprising administering dietary calcium or dairy induces a metabolic change, as

opposed to indirectly causing a dieter to lose weight.

The Examiner further asserts that as to the particular dosage frequency and amount, optimum parameters may be obtained by routine experimentation. This is incorrect hindsight analysis. It did in fact take extensive experimentation for the inventors to determine the claimed dosage frequency, amounts and vehicles as required by the present invention, as set forth in the specification and elsewhere, based on the discovery of the effects of calcium and dairy in inducing a metabolic change. For example, Example 1 involved at least six weeks of administration and Example 2 involved at least two six-week stages, all of which were followed by extensive analysis to arrive at the invention. Such experimentation, in complex long-term animal trials, is far from routine.

Also, the Examiner contends that one of ordinary skill will recognize that reduction in body fat content is a consequence of lipolysis of fat and recognize that obesity is a risk factor for coronary artery disease, and, therefore, loss of weight will reduce the risk of this disease. However, one would not be motivated to combine the teaching of Summerbell with this knowledge because as stated above, Summerbell only teaches weight loss through simple diets that can be easily adhere to. It does not advocate dairy or calcium as a general, possibly long term reducing diet for obese outpatients, because as Summerbell recognizes in the long term such a diet will cease to be novel and compliance will fall. This statement would lead one away from the present invention. Also, as discussed below the use of calcium or dairy in inducing a metabolic change was not previously recognized and would have been unexpected at the time the application was filed.

Moreover, the Examiner inappropriately takes official notice without documentary evidence to support the above conclusions. Official notice unsupported by documentary evidence

can not be taken by the Examiner where as here, the facts are not capable of instant and unquestionable demonstration as being well-known, and are in dispute (MPEP § 2144.03). As demonstrated by evidence submitted by the Applicant, as discussed below, the results of this invention, at the time the application was filed, were unexpected. For example, it would not have been commonly known to use calcium and dairy in amounts that are sufficient to avoid health problems, e.g., to induce a metabolic change or effect. Therefore, official notice as set forth by the Examiner that the claimed invention is obvious over allegedly well known elements is not permissible under these circumstances.

The Examiner has also rejected claims 1-4, 6-11 and 14 under U.S.C. § 103(a) as being unpatentable over Metz et al (AJH 1:58-60 1988). The Examiner asserts that Metz teaches a reduction in body fat in rats consuming higher diets of calcium and that it would have been obvious to one of ordinary skill to formulate a high calcium diet for humans to achieve the beneficial effect of a reduction in body fat content in view of the Metz results.

Applicants contend that the present invention is distinct from Metz, which does not disclose, teach or suggest any of the elements of independent claims 1, 7, 11 or 14.

Metz is directed to a hypothesis of testing the modification of body fat using the simultaneous administration of calcium with sodium. In the introduction, Metz teaches that some reports indicate supplementation of both dietary calcium and sodium results in a beneficial interaction between these two cations. The experiments were conducted on rats in three groups receiving: (1) high calcium/ high sodium, (2) moderate calcium/ moderate sodium and (3) low calcium/ low sodium. The results show that groups receiving higher amounts of calcium with sodium resulted in body weight reductions.

As set forth in the discussion, Metz teaches that "[t]o date, Ca^{2+} intervention trials in

humans with hypertension have not noted significant reduction in body weight with Ca^{2+} supplementation." Metz further teaches that: "[d]ietary sodium was simultaneously modified in this study, as earlier investigations had demonstrated that calcium effects on blood pressure were, in part, sodium-dependent. Thus, concurrent manipulations of Ca^{2+} and Na^{+} were utilized in this study." Metz concludes that "current results confirm that body fat and weight can be favorably modified by increasing the dietary content of both calcium and sodium."

Metz uses both "calcium and sodium" to show body weight changes. Metz does not isolate calcium from sodium and does not show or suggest that specifically only calcium or dairy is responsible for the weight benefits. A person of ordinary skill could not separate the effects of calcium from sodium based on Metz, and would not be motivated to do so based on the hypothesis of Metz: that calcium and sodium have synergistic effects on body fat and weight. To the contrary, the present invention specifically shows that calcium or dairy alone, without sodium, avoids health problems like coronary artery disease, e.g., because it induces metabolic change. Indeed, the use of two elements to allegedly effect body weight as in Metz, and the omission of one (sodium), while still retaining the function of a metabolic change as in the present invention, supports unobviousness of the present invention. See MPEP § 2144.04 ("the omission of an element and retention of its function is an indicia of unobviousness").

Therefore, Metz does not teach or suggest the use of calcium or dairy to induce a metabolic change as set forth in the present invention.

The Examiner further asserts that as to the particular dosage frequency, amount and vehicle, optimum parameters may be obtained by routine experimentation. As noted above, this point is incorrect.

Also, the Examiner contends that one of ordinary skill will recognize that reduction in

body fat content is a consequence of lipolysis of fat in adipocytes and recognize that obesity is a risk factor for coronary artery disease, and, therefore, loss of weight will reduce the risk of this disease. However, one would not be motivated to combine the teaching of Metz with this knowledge because sodium is known to be either neutral or damaging to various diseases such as coronary heart disease. It is not known as a beneficial agent for such disease, so there would be no motivation to administer calcium and sodium as set forth in Metz. Also, as discussed below the use of calcium or dairy in sufficient amounts to treat coronary disease, e.g. to induce a metabolic change or effect, were not previously recognized and would have been unexpected at the time the application was filed.

Moreover, as noted above, these points are incorrect, irrelevant to the pending claims and/or it was inappropriate for the Examiner to take official notice without documentary evidence to support these conclusions.

The present claims should not be deemed obvious in light of any of the cited references, Metz or Summerbell, because none of the cited references expressly or impliedly teach, disclose or suggest, any of the limitations set forth in present claims 1, 7, 11 or 14. Moreover, there is no motivation to use the cited knowledge, nor would combining the cited references or knowledge teach the claimed methods for avoiding or reducing a health problem, e.g., coronary artery disease, in an individual comprising administering sufficient amounts of dietary calcium or dairy to reduce the risk of a disease, e.g., to induce a metabolic change, e.g., to decrease intracellular calcium concentrations in adipocytes, stimulate lipolysis, inhibit lipogenesis, increase expression of white adipose tissue uncoupling protein 2 (UCP2), reduce serum insulin levels, increase thermogenesis, and/or decrease levels of calcitrophic hormones.

Therefore, Metz or Summerbell, either alone or in combination with other knowledge, do

not disclose, teach or suggest the claimed invention as set forth in claims 1, 7, 11 or 14 dependent claims 2-4, 6, and 8-10, which include additional limitations distinguishing them from the cited references. In claim 2, the method induces weight loss and/or prevents weight gain. In claim 4, the calcium is administered daily over a period of at least about six weeks, in an amount of at least about 1000 mg/day of dietary calcium. In claim 8, the dietary calcium is administered daily. In claim 9, the individual is a non-human mammal, and in claim 10, the method decreases intracellular calcium concentrations in adipocytes, stimulates lipolysis, inhibits lipogenesis, increases expression of white adipose tissue uncoupling protein 2 (UCP2), reduces serum insulin levels, increases thermogenesis, and/or decreases levels of calcitrophic hormones.

Therefore, claims 1-4, 6-11 and 14 are patentable because none of the cited references or materials disclose, teach or suggest the present invention.

Prior to the invention recited here, there was no recognition that calcium or dairy in food products or the diet would be beneficially or therapeutically effective to reduce or avoid health problems, such as coronary heart disease, in an individual at risk thereof due to excess body weight and/or an excess body fat, and therefore, the claimed methods could not have been obvious. The importance of maintaining high calcium intake and dairy during attempts to lose, maintain or control weight and thereby reduce or avoid health problems, such as coronary heart disease, in an individual at risk thereof due to excess body weight and/or an excess body fat was previously unrecognized and was unexpected prior to Dr. Zemel's team's pioneering work.

Due to these unexpected results, there has been a significant shift in the scientific community and the food industry, which has supported and endorsed the methods of the present invention. The inventive methods have achieved considerable public recognition and commercial success, as indicated by the attached documentation.

Page one of the attached material lists various clinical trials conducted by Dr. Zemel further showing the beneficial effects of consuming high calcium and dairy in accelerating the effects of weight loss in humans. Page two shows how the food industry has adopted the novel methods of the present invention. For example, the label "3-A-Day Milk Cheese Yogurt, Burn more fat, lose weight" communicates the message that increasing dairy consumption to at least three servings a day supports weight loss. As set forth on page two, over 50 top U.S. retail chains have licensed the inventive methods and are promoting the inventive methods by placing labels with the weight loss message on over 2.5 billion dairy packages to date. Pages three, four and five evidence various examples of leading industry packages and consumer advertisements. Page six provides testimonials about the inventive methods from notable health professional associations. The American Academy of Family Physicians refers to "dairy nutrition and its contribution to weight management." The National Medical Association recognizes that "[s]ome of the information that was presented today shows a clear beneficial relationship between the daily intake of three to four servings of dairy products and the reduction of obesity." The American Dietetic Association praises Dr. Zemel's work in that "[i]t has been exciting to see how emerging research on the role of calcium and dairy products adds to the body of knowledge about preventing and treating obesity [and t]his information provides additional tools for dietetics professionals to use in their day-to-day practice."

Applicants further contend that even with widespread recognition, the claimed method is so unexpected that there remains skepticism about the effects of calcium/dairy on weight loss. For example, there have been advertisements asserting that Yoplait yogurt promotes weight loss (advertising claims that are subject to a license agreement under the present patent application). A challenge was filed by an anonymous party, who argued that there was no support for the claim that calcium consumption promotes weight loss. The challenger apparently doubted the efficacy

of the invention as claimed in the present application. The National Advertising Division (NAD) of the U.S. Better Business Bureau ruled that the evidence (research by Dr. Zemel) supported General Mills' advertisement of the weight loss benefits of the calcium-containing dairy product (decision attached). This dispute, and its conclusion accepting the surprising evidence of the weight loss efficacy of calcium, further evidences the non-obviousness of the claimed invention. See also Express Article, published by Express Publications, a subsidiary of the Washington Post Company, 7/19/05, p. 10.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. Accordingly, Applicants request that the Examiner issue a Notice of Allowance indicating the allowability of claims 1-4, 6-11 and 14 and that the application be passed to issue. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

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